Oxone-promoted hydration of electron-deficient allenic esters and ketones into 1,3-dicarbonyl compounds

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ABSTRACT

A novel and mild protocol for the hydration of electron-deficient allenic esters and ketones into various 1,3-dicarbonyl compounds is described. The hydration of allenes promoted by oxone in DMF afforded the corresponding products in moderate to good yields. This work features the employment of only a catalytic amount of inexpensive and nontoxic solid reagent oxone ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$), avoiding the utility of toxic metals or traditional Brønsted acids, in a green version of viewpoint. A possible reaction mechanism for this transformation is also primarily proposed.

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Introduction

The hydration of unsaturated compound represents one of the most important and attractive method of C—O or C=O bond construction,[1] which is considered as a practical and totally atom-economical method in synthetic organic chemistry. The traditional mercury(II)-catalyzed hydration of alkynes has been proved to be a straightforward and effective method for the preparation of carbonyl compounds, but it was restricted in the industrial applications due to the high toxicity of the mercury derivatives.[1,2] Although many other metal catalysts, such as Fe,[3] Ru,[4] Ag,[5] Au,[6] and some Brønsted acid catalysts[7] have been studied and documented in recent years, it is still highly desirable to develop new catalytic systems and to broaden the diversity of substrates from both synthetic and environmental points of view.

Compared with the impressive development of alkynes' hydration, the hydration of allenes into carbonyl compounds was less well studied. The earlier studies focused on the Brønsted acid-catalyzed hydration of allenes, particularly the strong acid H_2SO_4 (Scheme 1, Eq. 1). However, this approach usually suffers from the relatively harsh reaction conditions and limited scope of allenes.[8] Wakatsuki and co-workers disclosed a Ru(II)-catalyzed hydration of mono-substituted allenes with the aid of a catalytic amount of CF_3COOH at elevated temperature, regardless of
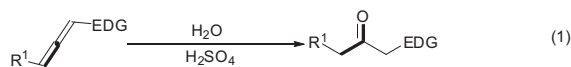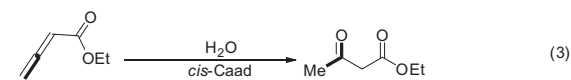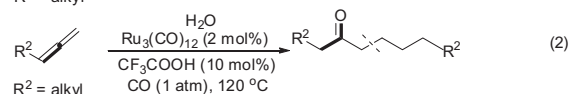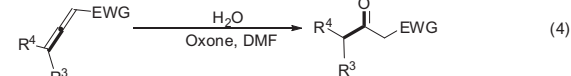

Scheme 1. Construction of C=O bond through the hydration of allenes.

affording the competitive hydrative dimerization and hydration product (Scheme 1, Eq. 2).[9] Very recently, Whitman and co-workers reported the hydration of 2,3-butadienoate to acetoacetate via an enamine intermediate in the presence of *cis*-3-chloroacrylic acid dehalogenase (*cis*-Caad), but the scope of this reaction remained to be investigated (Scheme 1, Eq. 3).[10] As part of our ongoing research programs of allenes,[11] herein, we report a general and efficient

Table 1
Optimization studies for the hydration of allenoate[a]
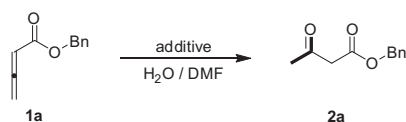
Entry	Additive (equiv)	Temp (°C)/time (h)	Yield[b] (%)
1	–	60/30	–
2	Oxone (1.5)	60/30	83
3	KHSO$_4$ (1.5)	60/30	65
4	CH$_3$COOH (1.5)	60/30	42
5	CF$_3$COOH (1.5)	60/30	75
6	TsOH·H$_2$O (1.5)	60/30	63
7	m-CPBA (1.5)	60/30	21
8	TBHP (1.5)	60/30	78
9	H$_2$O$_2$ (1.5)	60/30	45
10[c]	Oxone (1.5)	60/30	55
11[d]	Oxone (1.5)	60/30	57
12[e]	Oxone (1.5)	60/30	42
13	Oxone (1.0)	60/30	85
14	Oxone (0.5)	60/48	78
15	Oxone (1.0)	80/18	83
16	Oxone (0.5)	80/18	88
17	Oxone (0.5)	40/48	<10
18	Oxone (0.2)	80/30	75
19	Oxone (0.1)	80/30	73
20[f]	Oxone (0.5)	80/12	85

[a] Unless otherwise noted, all reactions were carried out with **1a** (0.2 mmol, 1.0 equiv) and H$_2$O (5.0 equiv) in DMF (2 mL).
[b] Isolated yield was obtained from an average of two runs.
[c] With recycled oxone.
[d] 10.0 equiv H$_2$O.
[e] A mixture solvent of DMF/H$_2$O (1:1).
[f] 0.5 mmol of **1a** was used.

method for the hydration of electron-deficient allenic esters and ketones into 1,3-dicarbonyl compounds (Scheme 1, Eq. 4). In comparison with the previously developed methods for the hydration of allenes, this new protocol employs milder conditions and affords the desired product with improved functional group tolerance. The methodology developed here prevented the utility of metal catalysts or traditional Brønsted acids, and only employed a catalytic amount of oxone in dimethylformamide (DMF) to trigger the reaction.

Results and discussion

In our initial research of oxidation of allenoate **1a**, the hydration product β-keto ester **2a** was separated unexpectedly in the assistance of oxone (Table 1, entry 2). This result encouraged us to further study the hydration of allenoates avoiding the use of heavy metals. The reason that oxone was effective for this transformation may be due to its acidity, then some traditional Brønsted acids as well as some other acidic peroxides were screened for the reaction (Table 1, entries 3–10). Among all these acidic additives, the inexpensive and nontoxic reagent oxone showed the highest efficiency to give the desired product in 83% yield, which was chosen as the additive for next reaction condition optimization. It should be noted that KHSO$_4$ could also effectively promote this transformation. In addition, oxone could be easily recovered by filtration or centrifugation and reused for this hydration reaction, albeit a loss of hydration activity (Table 1, entry 11).

Subsequent screening of solvents exhibited the remarkably dominant role of DMF in this reaction, because rare reaction occurred in other solvents, such as dimethylacetamide (DMA), dichloromethane, dimethylsulfoxide (DMSO), acetonitrile, toluene, and 1,4-dioxane. It should be noted that the amount of H$_2$O
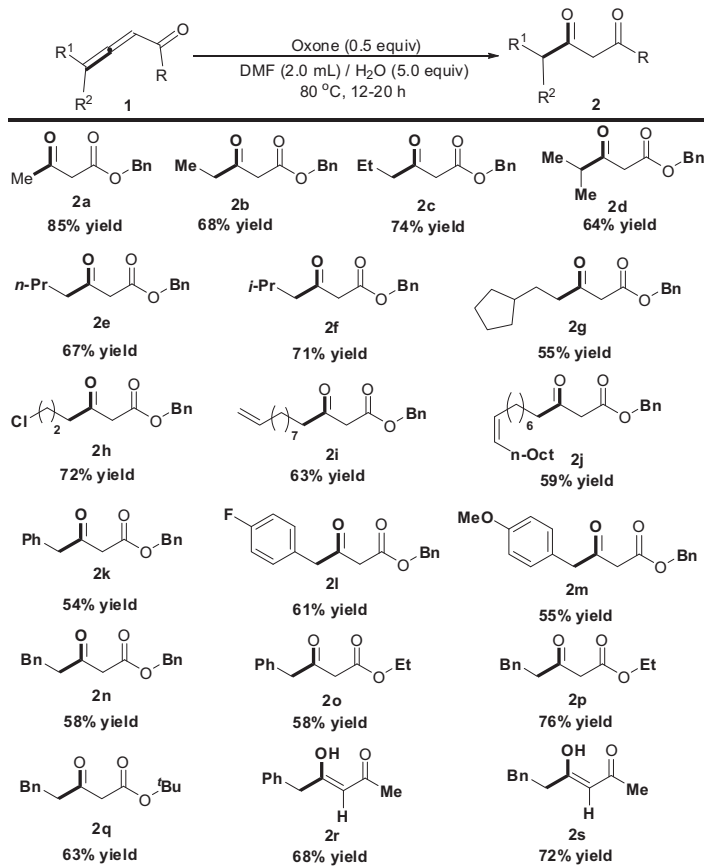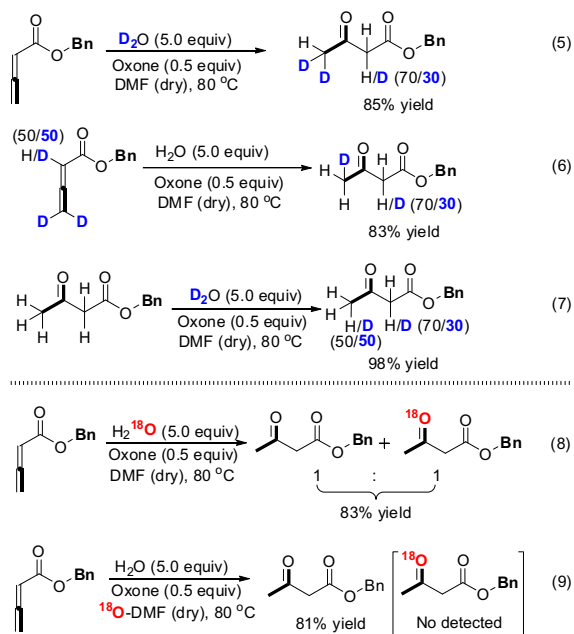

Scheme 2. Hydration of allenic esters and ketones to 1,3-dicarbonyl compounds. All reactions were carried out with **1** (0.5 mmol). Isolated yield was obtained from an average of two runs.

showed an important role in this transformation. The best result could be achieved when 5.0 equiv water were used. Further increasing the ratio of water led to a decrease of the yield of **2a**, and when a mixing solvent of DMF/H$_2$O (1:1) was used, the yield of **2a** decreased to 42% (Table 1, entries 11 and 12). Then the additive amount and temperature were further optimized (Table 1, entries 13–19), and the yield of the product **2a** could be improved to 88% at 80 °C employing only 0.5 equiv oxone. Finally, this transformation was large-scaled to 0.5 mmol of **1a** in the presence of DMF (2 mL) with 5 equiv H$_2$O, furnishing the product with a valuable yield of 85% (Table 1, entry 20).

With the optimized reaction conditions in hand, a variety of allenic esters and ketones were synthesized to investigate the scope of this reaction. As depicted in Scheme 2, a wide range of electron-deficient allenoates bearing different substituents at γ-position, including alkyl, cyclic alkyl, and alkenyl groups, could be transformed into corresponding products (**2a–j**) in 54–85% isolated yields. For allenoate with two methyl groups at the γ-position, the corresponding γ-disubstituted product **2d** could be obtained in 64% yield. Particularly, it is of considerable utility that compounds **2h–j** were synthesized in good yields regardless of the functional groups like alkenyl and Cl atom, which may be potentially used in further alterations. A series of γ-benzyl or aryl-substituted allenoates were also examined through this approach. The introduction of electron-withdrawing and electron-donating groups on the aryl rings had little influence on the yield of the reaction. The corresponding products **2k–q** were obtained in moderate to good yields. Also, allenoates with different ester moieties (including Bn, Me, Et, and ^{t}Bu) were capable to furnish this reaction. Furthermore, two allenic ketones were also subjected to this transformation under the same conditions, thus giving rise to the relatively stable enol products **2r** and **2s** in 68% and 72% yields, respectively. In addition, we investigated the hydration reaction with α-substituted allenoates, such as ethyl 2-methylbuta-2,3-dienoate and ethyl 2-benzylbuta-2,3-dienoate. These substrates were found to be unsuitable for this hydration transformation and no desired products were observed.

To get more insights into this transformation, a series of isotopic labeling and controlling experiments were performed under
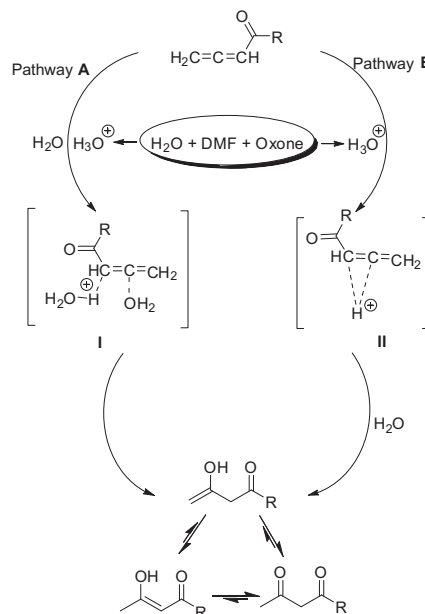

Figure 1. Proposed pathways for oxone-promoted hydration of allenic esters and ketones.

the standard reaction conditions (Scheme 3). Deuterium-labeled experiments indicated that the hydrogen atom introduced at the α-position of the product could be possibly originated from H$_2$O or oxone (Eq. 5). The proton exchange between the product and H-donors was quite possible due to the enol tautomerism of the product (Eqs. 6 and 7). Subsequently, by using ^{18}O-labeled H$_2$O, we were delighted to find compelling evidence that the oxygen atom is derived from water, as the ^{18}O-labels was effectively incorporated into the product (Eq. 8). In the presence of ^{18}O-labeled DMF, however, the ^{18}O-labeled product was not detected by the MS analysis (Eq. 9). Thus, the observed DMF effect may be due in part to the relative solubility of oxone.

Based on the above results and some related literature,[12] two possible pathways (**A** and **B**) for this hydration reaction are illustrated in Figure 1. Initially, DMF may react with oxone to give the activated hydrogen proton, which may then activated the allene to form a concerted complex **I** or a π-complex **II**. Subsequent transformation of complexes **I** and **II** yields enol isomers, which undergo enol tautomerism to afford the desired product.

Conclusion

In summary, we have successfully developed a metal-free and general protocol for the hydration of electron-deficient allenic esters and ketones. A series of 1,3-dicarbonyl compounds can be accessed in moderate to good yields under the mild reaction conditions. The use of oxone as the additive makes this transformation both economical and environmentally sound. Efforts to the extension of this method to other substrates as well as the further mechanistic studies are continuing in our laboratory.

Experimental section

General procedure for the hydration of electron-deficient allenic esters and ketones: To a solution of the oxone (0.5 equiv) in DMF (2 mL) was added allene (0.5 mmol, 1.0 equiv), and then H$_2$O (5.0 equiv) was added dropwise to the system. The reaction mixture was transferred to an 80 °C oil bath and conducted at the

Scheme 3. Preliminary mechanism studies.

indicated temperature for the stated time. After the reaction was completed and cooled to room temperature, 5 mL water was added and extracted with EtOAc (8 mL × 3) to remove most of DMF. The organic phases were collected, washed with saturated brine to remove the residual DMF, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Purification by flash chromatography on silica gel (petroleum/ethyl acetate = 50:1 to 20:1) afforded the corresponding product.

Acknowledgments

Supplementary data

Supplementary data (general experimental details, lists of spectral data, images of ^1H, ^{19}F and ^{13}C NMR spectra for all compounds) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2015.05.120.

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